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10/529,064	08/02/2005	Pierre Michel Desmons	B45308	4877

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EXAMINER	
GANGLE, BRIAN J	
ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/529,064	DESMONS ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7 and 11-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and remarks, filed 11/9/2007, are acknowledged. Claims 1, 6, and 11-14 are amended. Claims 1, 6-7, and 11-14 are pending. Claims 11-14 are withdrawn as being drawn to non-elected inventions. Claims 1, 6, and 7 are currently under examination.

Claim Objections

Claims 1, 6, and 7 are objected to because of the following informalities: claim 1 recites the serosubtype "B:4:P1.7,b,4." Based on the serosubtype designations used in the art and the specification, the comma immediately after the 7 should be removed so that the serosubtype is "B:4:P1.7b,4." Appropriate correction is required.

Claim Rejections Withdrawn

The rejection of claim 6 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "vaccine for the treatment of," is withdrawn in light of applicant's amendment thereto.

The rejection of claims 1-9 under 35 U.S.C. 102(b) as being anticipated by Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) is withdrawn in light of applicant's amendment to include the strain B:4P1.7b,4.

The rejection of claims 1-9 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Granoff *et al.* (PCT Publication WO 02/09643, 2/7/2002), is withdrawn in light of applicant's amendment to include the strain B:4P1.7b,4.

The rejection of claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) in view of Lehmann *et al.* (APMIS 99:769-772, 1991), is withdrawn in light of applicant's amendment to include the strain B:4P1.7b,4.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 6-7 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for multivalent vaccines providing protection against *Neisseria meningitidis*, does not reasonably provide enablement for multivalent vaccines for protection against neisserial disease, is maintained for essentially the reasons set forth in the rejection of claims 6-10 in the previous office action. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has not addressed this rejection in their remarks. In the previous office action, there were two issues presented in the enablement rejection. First, the claims were not enabled for vaccines that provided treatment. Applicant's amendment has resolved this issue, as the claims are now drawn to vaccines for protection against meningococcal disease. The second issue is that the claims encompass protection against all neisserial disease. As stated previously (and reiterated below), one of skill in the art would have no expectation that a vaccine comprising meningococcal components would provide protection against any neisserial disease other than those caused by *Neisseria meningitidis*. This portion of the rejection is maintained.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about

the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to vaccines for protection against neisserial disease. Said vaccines contain blebs that are deficient in PorA, derived from the *Neisseria meningitidis* B CU-385 strain and blebs that are not deficient in PorA, derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand.

Breadth of the claims: The claims encompass prevention of all diseases caused by bacteria of the genus *Neisseria*. This included meningitis (caused by *Neisseria meningitidis*), gonorrhea (caused by *Neisseria gonorrhoeae*), as well as opportunistic infections caused by other species within the genus.

Guidance of the specification/The existence of working examples: The specification does not disclose any challenge experiments with any bleb compositions to show prevention of any neisserial disease. The specification does refer to work in the art with the so-called Norwegian and Cuban vaccine strains, as well as a New Zealand strain.

State of the art: The Norwegian and Cuban strains are accepted to be effective in preventing meningitis caused by *Neisseria meningitidis* (Granoff *et al.* WO 02/09643; Lehmann *et al.*, APMIS 99:769-772, 1991; Rodriguez *et al.*, Mem. Inst. Oswaldo Cruz, 94:433-440, 1999). Vaccines against the New Zealand epidemic strain (B:4:P1.7b,4) are also known to be effective (Vermont *et al.*, Infect. Immun., 70:584-590, 2002). There is no evidence in the art that a vaccine containing antigens from *Neisseria meningitidis* would have any effect whatsoever on diseases caused by other bacteria in the genus *Neisseria*.

Therefore, in view of the lack of support in the art and specification for vaccines for protection against neisserial disease, it would require undue experimentation on the part of the

skilled artisan to make and use the vaccine as claimed; therefore the full scope of the claims is not enabled.

New Claim Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) in view of Vermont *et al.* (Infect. Immun., 70:584-590, 2/2002) and Baker *et al.* (J. Paediatr. Child Health, 37:S13-S19, 2001).

The instant claims are drawn to a multivalent bleb composition comprising a first bleb composition comprising a first bleb preparation deficient in PorA, derived from the *Neisseria meningitidis* B CU-385 strain and a second bleb preparation that is not deficient in PorA, derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand (claim 1); a vaccine for protection against neisserial disease comprising said bleb composition and a pharmaceutically acceptable excipient (claim 6); and a vaccine for protection against neisserial disease comprising said bleb composition and a pharmaceutically acceptable excipient and one or more plain or conjugated meningococcal capsular polysaccharides selected from the group of serogroups A, C, Y, and W (claim 7).

Berthet *et al.* disclose a multivalent vaccine comprising mixtures of meningococcus bleb preparations as well as a pharmaceutically acceptable excipient (see page 36, lines 5-28 and page 33, lines 1-5). Said vaccine comprises mixtures of bleb preparations from 2 or more strains, including serotypes P1.15, P1.7,16, and P1.4 (see page 36, lines 15-19). Said vaccine is also disclosed as comprising any or all of the capsular polysaccharides A, C, Y, or W (see page 36, lines 11-14). Berthet refers to compositions that should be protective against strain CU-385

(page 35, lines 17-30). It is noted that, according to the instant specification, strain CU-385 is deficient in PorA (see page 22, lines 19-22 and page 24, lines 8-11)

Berthet differs from the instant invention in that they do not disclose a composition that comprises blebs from CU-385 in combination with blebs from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand.

Vermont *et al.* disclose an outer membrane vesicle (blebs) vaccine that comprises blebs from a meningococcal strain which has the serosubtype P1.7-2,4 (which is the epidemic serosubtype prevalent in New Zealand) (page 584, column 2, paragraph 1 and page 585, column 1, paragraph 4). As evidenced by Oster (WO 2006/024946, 2006) and Martin *et al.* (Clin. Vacc. Immunol., 13:486-491, 2006), there are different nomenclature systems in use with regard to *Neisseria meningitidis* serosubtypes. According to the different nomenclature systems, serosubtype P1.7-2,4 is the same serosubtype as P1.7b,4.

Baker *et al.* disclose information on the meningococcal disease epidemic in New Zealand. They show that the majority of the strains isolated during the epidemic were B:4:P1.7b,4 (see abstract). Baker *et al.* also suggest that a vaccine that could induce immunity to this strain would be useful in controlling the epidemic (page S18, column 1, paragraph 4).

It would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the bleb preparation from serosubtype P1.7-2,4, as disclosed by Vermont *et al.* in the multivalent bleb vaccine along with a bleb preparation of CU-385 as disclosed by Berthet *et al.* for several reasons. Baker *et al.* state that a vaccine that protects against serosubtype P1.7-2,4 would help to control the New Zealand meningococcus epidemic. In addition, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, the multivalent bleb composition against CU-385 is taught by Berthet *et al.* to be useful in protection against meningococcal disease and the vaccine of Vermont *et al.* is taught to be useful in protection against meningococcal disease. Therefore, it would have been obvious to combine the two vaccines into a single multivalent vaccine. Finally, according to the

Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. In this case, vaccines containing blebs from each strain were known in the art, each of these elements would have performed the same function as they would have separately and the results of the combination would have been predictable.

One would have had a reasonable expectation of success because blebs from these strains have been shown to be effective as separate vaccines.

Claims 1, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Granoff *et al.* (PCT Publication WO 02/09643, 2/7/2002) in view of Vermont *et al.* (Infect. Immun., 70:584-590, 2/2002) and Baker *et al.* (J. Paediatr. Child Health, 37:S13-S19, 2001).

The instant claims are drawn to a multivalent bleb composition comprising a first bleb composition comprising a first bleb preparation deficient in PorA, derived from the *Neisseria meningitidis* B CU-385 strain and a second bleb preparation that is not deficient in PorA, derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand (claim 1); a vaccine for protection against neisserial disease comprising said bleb composition and a pharmaceutically acceptable excipient (claim 6); and a vaccine for protection against neisserial disease comprising said bleb composition and a pharmaceutically acceptable excipient and one or more plain or conjugated meningococcal capsular polysaccharides selected from the group of serogroups A, C, Y, and W (claim 7).

Granoff *et al.* disclose an outer membrane vesicles (bleb) vaccine that comprises a mixture of blebs from genetically diverse strains of *Neisseria meningitidis* as well as a pharmaceutically acceptable excipient (see page 6, lines 23-31 and page 22, lines 5-20). Granoff *et al.* also disclose a bleb vaccine that contains a mixture of blebs from a serogroup C strain as well as a strain with the serogroup P1.4 (see page 7, lines 19-27). Figure 1 discloses a vaccine with the serosubtype B:4:P1.15, that was used in Cuba and Brazil from 1987-1991. Granoff, on page 14, refers to an OMV vaccine prepared by the Finley Institute in Cuba which has been given to millions of children in South America. It is clear from an examination of the art and the

instant specification, that CU-385 (commonly referred to as the Cuban strain) is the strain referred to in Granoff on page 14 and in Figure 1. Additionally, Granoff *et al.* disclose that the disclosed mixture vaccine has the advantage of broad spectrum protective immunity (see page 15, lines 10-12).

Granoff *et al.* do not explicitly disclose that the bleb vaccine mixture should contain the strain CU-385 and a B:4:P1.7b,4 strain.

Vermont *et al.* disclose an outer membrane vesicle (blebs) vaccine that comprises blebs from a meningococcal strain which has the serosubtype P1.7-2,4 (which is the epidemic serosubtype prevalent in New Zealand) (page 584, column 2, paragraph 1 and page 585, column 1, paragraph 4). As evidenced by Oster (WO 2006/024946, 2006) and Martin *et al.* (Clin. Vacc. Immunol., 13:486-491, 2006), there are different nomenclature systems in use with regard to *Neisseria meningitidis* serosubtypes. According to the different nomenclature systems, serosubtype P1.7-2,4 is the same serosubtype as P1.7b,4.

Baker *et al.* disclose information on the meningococcal disease epidemic in New Zealand. They show that the majority of the strains isolated during the epidemic were B:4:P1.7b,4 (see abstract). Baker *et al.* also suggest that a vaccine that could induce immunity to this strain would be useful in controlling the epidemic (page S18, column 1, paragraph 4).

It would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the bleb preparation from serosubtype P1.7-2,4, as disclosed by Vermont *et al.* in the multivalent bleb vaccine along with a bleb preparation of CU-385 as disclosed by Granoff *et al.* for several reasons. Baker *et al.* state that a vaccine that protects against serosubtype P1.7-2,4 would help to control the New Zealand meningococcus epidemic. In addition, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, a bleb composition against CU-385 is taught by Granoff *et al.* to be useful in protection against meningococcal disease and the vaccine of Vermont *et al.* is taught to be useful in protection against meningococcal disease. Therefore, it would have been obvious to

combine the two vaccines into a single multivalent vaccine. Finally, according to the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. In this case, vaccines containing blebs from each strain were known in the art, each of these elements would have performed the same function as they would have separately and the results of the combination would have been predictable.

One would have had a reasonable expectation of success because the strains have been shown to be effective as separate vaccines.

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the phrase "a first bleb preparation deficient in PorA derived from the *Neisseria meningitidis* B CU-385 strain." It is not clear whether it is the bleb preparation that is derived from the *Neisseria meningitidis* B CU-385 strain or whether it is PorA that is derived from the *Neisseria meningitidis* B CU-385 strain. This rejection affects all dependent claims.

Claim 1 is rendered vague and indefinite by the phrase "a second bleb preparation that is not deficient in PorA derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand." It is not clear whether it is the bleb preparation that is derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand or whether it is PorA that is derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand. This rejection affects all dependent claims.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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